1,2,4-Thiadiazole 4-oxides

Lidia S. Konstantinova,[a] Oleg A. Rakitin,[a] Charles W. Rees,[b] Tomás Torroba,[c] Andrew J. P. White[b] and David J. Williams[b]

[a] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky Prospekt 47, Moscow 117913, Russia*
[b] *Department of Chemistry, Imperial College of Science, Technology and Medicine, London, UK SW7 2AY*
[c] *Departamento de Química, Facultad de Ciencias, Universidad de Burgos, 09001 Burgos, Spain*

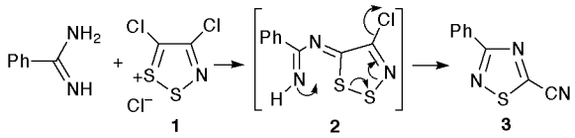
Received (in Cambridge) 2nd June 1999, Accepted 23rd June 1999

Benzamidine reacts with 4,5-dichloro-1,2,3-dithiazolium chloride **1** to give 5-cyano-3-phenyl-1,2,4-thiadiazole **3**. Similarly, benzamidoxime† reacts with **1** regiospecifically to give 5-cyano-3-phenyl-1,2,4-thiadiazole 4-oxide **5**, the first 1,2,4-thiadiazole *N*-oxide, as a minor product. *O*-Acylbenzamidoximes **8b–e** give the same *N*-oxide **5** in somewhat better yield, the best being from the *N*-methylcarbamate **8e** (30%). The derivative **10** of other benzamidoximes, with electron releasing substituents gives the analogous 5-cyano-3-aryl-1,2,4-thiadiazole 4-oxides **11** in comparable yield. The *N*-oxides are shown to be the 4-isomers by analysis of the NMR and mass spectra of ^{15}N-labelled and unlabelled products and X-ray structure determination of the derived carboxamide **14**. This suggests a mechanism in which the amidoximes react with **1** *via* their oximino, rather than amino, nitrogen atom. Such a mechanism is supported by the isolation of benzonitrile and the novel benzoyloxyiminodithiazole **13** as by-products in the reaction of *O*-benzoylbenzamidoxime **8c** with **1**. Thiadiazole **3** has an almost planar structure in the solid state, and the packing of the molecules is controlled by cooperative electrostatic, dipole · · · dipole, π–π, and aromatic edge-to-face interactions. Compound **13** also has a near-planar conformation and a packing motif exhibiting O · · · S electrostatic interactions and π–π stepped stacks. In **14** there are only small out-of-plane torsional twists and the packing is dominated by N–H · · · O hydrogen bonds, weak S · · · N interactions and π–π stacking of loosely linked tapes.

N-Oxides of five membered heterocycles are relatively rare,[1] especially when they contain sulfur since direct oxidation usually gives *S*-oxides, as for example with 1,2,5-thiadiazoles.[2] In spite of the many applications of 1,2,4-thiadiazoles as biologically active compounds in agriculture and medicine, as dyestuffs, lubricant additives and vulcanization agents,[3] *N*- and *S*-oxides appear not to have been reported for this ring system, apart from our preliminary communication of the present results.[4] We have discovered a simple method for the preparation of *N*-oxides of 1,2,4-thiadiazoles by condensation of benzamidoximes[5] with 4,5-dichloro-1,2,3-dithiazolium chloride (Appel salt) **1**.[6]

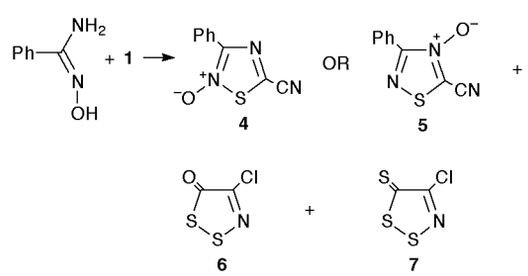
The ready preparation of Appel salt from chloroacetonitrile and disulfur dichloride and its high reactivity have resulted in the synthesis of various heterocycles such as 2-cyanobenzothiophenes, benzothiazoles, benzimidazoles and benzoxazoles.[7] The salt **1** reacts rapidly with primary aromatic amines to give 5-arylimino-1,2,3-dithiazoles which yield 2-cyanobenzothiazoles on heating.[7c] It also reacts with benzamidine but the analogous 5-imino derivative **2** collapses spontaneously at room temperature to give 5-cyano-3-phenyl-1,2,4-thiadiazole **3** in low yield (23%) (Scheme 1), together with 4-chloro-1,2,3-dithiazole-5-thione **7** (64%).[7a,8] The structure of **3** was confirmed by X-ray crystallography. If benzamidoxime were to react with **1** in the same way the product would be an *N*-oxide of thiadiazole **3**; the 2-oxide **4** is the strictly analogous product, but the 4-oxide **5** could also be formed.

Treatment of benzamidoxime with Appel salt **1** in DCM at room temperature, followed by stirring with pyridine, gave the 4-oxide **5** (see below) in very low yield (8%) as reasonably stable



Scheme 1

colourless crystals, mp 142–144 °C, together with 4-chloro-1,2,3-dithiazol-5-one **6** (32%) and 5-thione **7** (15%) which are common by-products in reactions of the salt **1** (Scheme 2).



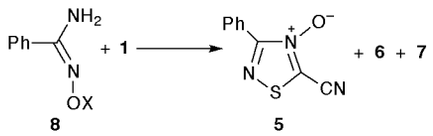
Scheme 2

The structure of product **5** as one of the possible oxides of thiadiazole **3** was confirmed by its ready deoxygenation by triphenylphosphine in DCM at room temperature to give **3** in high yield.

In an attempt to improve the yield of the thiadiazole *N*-oxide, various known *O*-substituted benzamidoximes **8a–e** (Table 1) were prepared and treated with salt **1** in DCM at room temperature, followed by the addition of pyridine. Curiously the

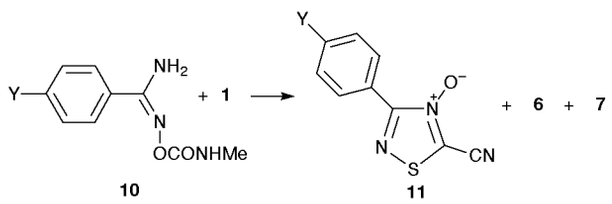
† IUPAC name: benzamide oxime.

Table 1 The reaction of benzamidoximes **8** with Appel salt **1** in DCM at room temperature



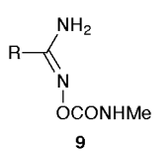
	Yield (%)					
	X					
Product	H	**a** TMS	**b** Ac	**c** Bz	**d** 4-ClBz	**e** CONHMe
5	8	0	22	20	25	30
6	32	70	12	5	21	25
7	15	5	5	trace	5	10

Table 2

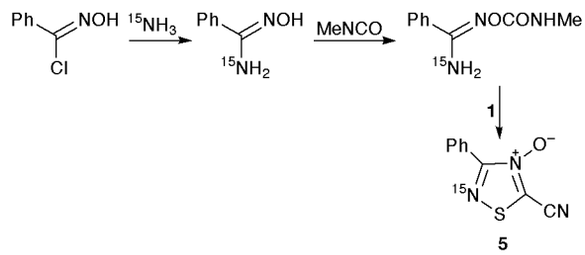


	Yield (%)		
	Y		
Product	**a** Me	**b** OMe	**c** NMe_2
11	26	29	21
6	10	8	10
7	15	12	18

O-TMS derivative gave no *N*-oxide, but the *O*-acetyl, benzoyl, 4-chlorobenzoyl and methylcarbamoyl derivatives all gave the same *N*-oxide in somewhat higher yield (20–30%) together with comparable amounts of dithiazolone **6** and dithiazolethione **7**, as shown in Table 1. Since the best yield of the *N*-oxide was obtained from the methylcarbamoyl derivative **8e**, we used this derivative of other amidoximes to explore the scope of the reaction and to determine the reaction pathway by ^{15}N-labelling. The reaction scope proved to be quite limited. Alkylamidoximes **9** (R = Me, Bu^t, Bn) and arylamidoximes with electron

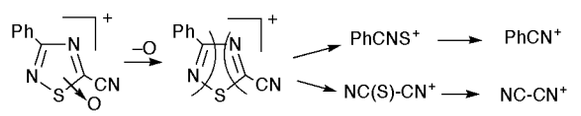


withdrawing substituents **10** (Y = Cl, Br, NO_2 and the 3-NO_2 isomer) (Table 2) did not give *N*-oxides, but only the dithiazolone **6** (up to 38%) and dithiazolethione **7** (up to 60%), often in high combined yield. However, with **10** (Y = Me, OMe, NMe_2) the corresponding *N*-oxides **11** were isolated, together with **6** and **7**, as shown in Table 2. The close similarity of the IR, ^{13}C NMR and mass spectra of the thiadiazoles **11a–c** with each other and with the phenyl compound **5** (see Experimental section) indicated that all four products were similar in structure and were presumably oxygenated on the same nitrogen atom. The site of oxidation was established as follows. The methylcarbamoyl derivative **8e** was specifically labelled with ^{15}N (94% ^{15}N) as shown in Scheme 3, and treated with Appel salt **1** exactly as before to give an *N*-oxide (30%, 91% ^{15}N). This was shown to be isomer **5** by analysis of the NMR and mass spectra of labelled and unlabelled products. In the ^{15}N NMR spectrum



Scheme 3

of the *N*-oxide there is only one signal, corresponding to the unoxidized nitrogen atom of the thiadiazole ring, at δ −110.9 ppm. In the ^{14}N NMR spectrum the *N*-oxide nitrogen signal is at δ −70.7 ppm (half height width $\Delta\nu_{1/2}$ = 76.5 Hz), characteristic of heterocyclic *N*-oxides. Thus all the ^{15}N label is on the unoxidized ring nitrogen atom. In the mass spectrum of unlabelled *N*-oxide the first fragmentation was loss of the oxygen atom, followed by the fragmentation observed for the deoxygenated compound **3** which is the usual fragmentation of the 1,2,4-thiadiazole ring (Scheme 4).[9] The mass spectrum



Scheme 4

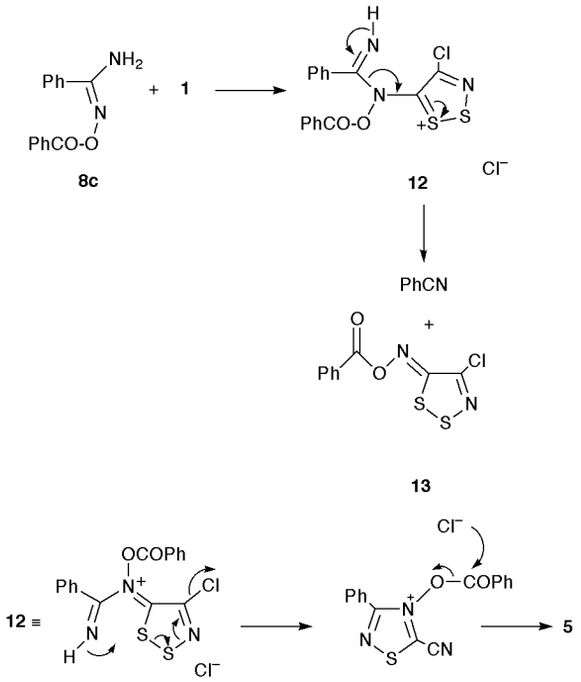
showed that all the label resides on the 2-nitrogen atom linked to sulfur [peaks for PhC^{15}NS (*m*/*z* 136) and PhC^{15}N (*m*/*z* 104)], and the 4-nitrogen is completely unlabelled [peaks for NC(S)–CN (*m*/*z* 84) and NC–CN (*m*/*z* 52)]. This proves that the product is the 4-oxide **5**. Additional support for this structure came from the ^{13}C NMR of the labelled compound. For geminal ^{13}C–C–^{15}N interactions the proximity of the nitrogen lone pair to the β-carbon atom greatly enhances the coupling constant (^2J = 9–10 Hz).[10] With our product the ^{15}N does indeed couple strongly to the *ipso*-carbon of the phenyl ring (^2J = 5.2 Hz), but does not couple to the cyanide carbon as would be expected for the 2-oxide **4**.

We have observed many reactions of the reagent **1** with primary amines bearing another nucleophilic centre to proceed through a 5-iminodithiazole intermediate followed by cyclization of the second nucleophile onto S-1 (*cf*. Scheme 1) or C-5 of the dithiazole ring.[11] A new cyano-substituted 6- or 5-membered ring is formed with the loss of one or two sulfur atoms, respectively. If the amidoximes react with **1** in this general way, as we believe, then formation of the 4-oxides **5** and **11** requires that initial attack by the amidoxime group occurs through the oximino nitrogen atom to give intermediate **12** in Scheme 5. Somewhat surprisingly there was no evidence for the formation of any 2-oxide isomers, which would result from initial attack through the primary amino group.

The former pathway (Scheme 5) explains the isolation of two other products from the reaction of *O*-benzoyl benzamidoxime **8c**; these were benzonitrile (23%) and the stable benzoyloxyimine **13** (15%). All three products are derivable from the initial intermediate **12** in Scheme 5, which shows how the 4-oxide **5** is thought to be formed.

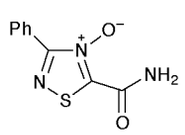
The novel benzoyloxyimine **13** was prepared independently in 34% yield from *O*-benzoylhydroxylamine and Appel salt **1** in DCM at room temperature followed by the addition of pyridine. Its structure was confirmed by a single crystal X-ray study (see below). Attempts to hydrolyse **13** to the 5-hydroxyiminodithiazole with aqueous ethanolic sodium hydroxide or hydrochloric acid gave only benzoic acid, sulfur and gaseous products.

The 5-cyano-1,2,4-thiadiazole 4-oxides **5** and **11** formed colourless to pale yellow crystals of only moderate stability, and



Scheme 5

unfortunately not of X-ray diffraction quality. They decomposed slowly in solution or as solids at room temperature, and rapidly in boiling toluene to give the deoxygenated 1,2,4-thiadiazole. They were sufficiently stable to flash chromatography to be isolated and purified in this way with reasonable recovery. The oxide **5** was unstable in alkaline solution but was cleanly hydrolysed by hot dilute hydrochloric acid to the amide *N*-oxide **14** which was much more stable than **5**, presumably owing to intramolecular H-bonding. The structure of **14**, and hence of **5**, was proved by X-ray crystallography.



14

It is worth noting that neither the oxide **5**, nor any other oxide, was produced in a brief study of the direct oxidation of thiadiazole **3**. Thiadiazole **3** did not react with MCPBA in DCM at room temperature, and was slowly decomposed by this mixture upon heating; it was also decomposed by trifluoroperacetic acid at room temperature.

The X-ray analysis of **3** shows (Fig. 1) the molecule to be almost planar with only a *ca*. 2° torsional twist about the bond linking the thiadiazole and phenyl ring systems. The pattern of bonding within the thiadiazole ring is consistent with the presence of formal N=C double bonds for the N(2)–C(3) and N(4)–C(5) linkages, though there is some evidence for delocalization that extends from S(1) *via* C(3) to C(5). There are several examples of structurally characterized thiadiazoles in the literature, and two in particular [1,2,4-thiadiazole-3,5-dicarbonitrile[12] and 3-(4-bromophenyl)-5-chloro-2,4-diazathiophene[13]] are appropriate for comparison. In both of these structures the pattern of bonding is remarkably similar to that observed in **3**, indicating that the nature of the substituent on C(3) has little effect on the bonding within the ring.

Inspection of the packing of the molecules reveals several features of interest. Centrosymmetrically related pairs of molecules are aligned head-to-tail to form pseudo-dimers that are linked *via* a combination of i) dipole···dipole and π–π interactions between the cyano groups (**a** in Fig. 2) and ii) electrostatic S···N interactions between the ring sulfur and the cyano nitrogen (**b** in Fig. 2). These "dimers" are then stacked, a phenyl ring of one dimer overlaying a thiadiazole ring of another (**c** in Fig. 2). These stacks are then aligned head-to-head to produce a chevron-like array that is stabilized by aromatic···aromatic edge-to-face interactions (**d** in Fig. 2). It is interesting to note that in the structure of 1,2,4-thiadiazole-3,5-dicarbonitrile there are neither stacking nor C≡N···N≡C dipole···dipole interactions, though there is a short S···N≡C contact of 3.05 Å.[12]

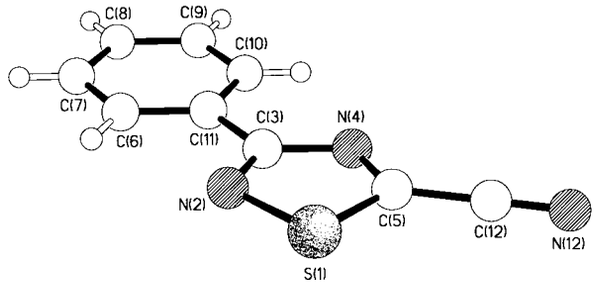


Fig. 1 The molecular structure of **3**. Selected bond lengths (Å) are: S(1)–N(2) 1.635(2), S(1)–C(5) 1.708(2), N(2)–C(3) 1.325(2), C(3)–N(4) 1.371(2), C(3)–C(11) 1.468(2), N(4)–C(5) 1.305(3), C(5)–C(12) 1.437(3), C(12)–N(12) 1.134(3).

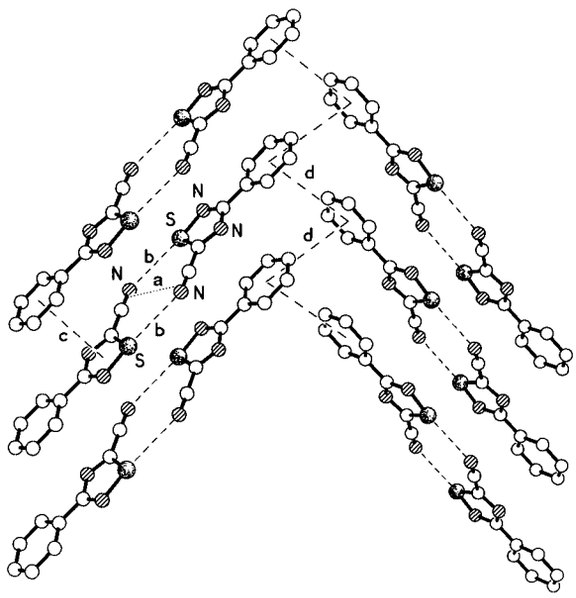


Fig. 2 The chevron-like array formed by stacked "dimer pairs" of **3**. The intermolecular contacts are: (**a**) the perpendicular separation between the C≡N bonds is 3.25 Å; (**b**) the S···N distance is 3.22 Å; (**c**) the centroid···centroid and mean interplanar separations are 3.66 and 3.39 Å respectively (the ring systems are inclined by *ca*. 3°); (**d**) the centroid···centroid separation is 4.96 Å.

The single crystal study of **13** confirmed the dithiazole nature of the heterocycle (Fig. 3). The molecule has a near planar conformation [to within 0.12 Å for Cl(4)], the largest torsional twist about the backbone linking the two ring systems being 174.7(3)° about N(6)–O(7). Structurally characterized dithiazole ring systems are rare, there being only two pendant (*i.e.* non-fused) examples to date, namely [3-chloro-4-(4-chloro-5*H*-1,2,3-dithiazol-5-ylimino)-1,2,5-thiadiazolium-2-yl]pentafluoroarsenate sulfur dioxide[14] and 4-chloro-1,2,3-dithiazolium-5-yl 4-methylphenolate,[6] that have been reported. Both of these have patterns of bonding which are essentially identical to those we observe in **13** despite the very different natures of the substituent on C(5).

The packing of molecules of **13** exhibits two distinctive motifs, i) polar chains of molecules linked *via* a pair of asym-

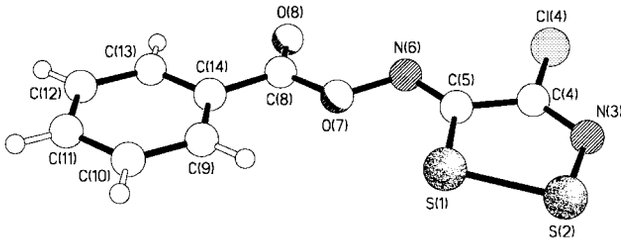


Fig. 3 The molecular structure of **13**. Selected bond lengths (Å) are: S(1)–C(5) 1.740(4), S(1)–S(2) 2.079(2), S(2)–N(3) 1.659(4), N(3)–C(4) 1.264(5), C(4)–C(5) 1.456(5), C(4)–Cl(4) 1.715(4), C(5)–N(6) 1.276(5), N(6)–O(7) 1.445(4).

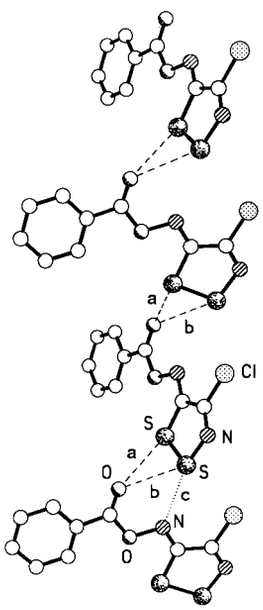


Fig. 4 Part of one of the electrostatically linked polar chains of molecules present in the crystals of **13**. The intermolecular contacts are: (**a**) 2.93; (**b**) 3.12; (**c**) 3.42 Å.

metric electrostatic O · · · S interactions (**a** and **b** in Fig. 4) which in turn form ii) stepped stacks of C_i-related head-to-tail "dimers" (Fig. 5).

The X-ray structure of **14** shows (Fig. 6) that this molecule too has a nearly planar conformation, the torsional twists about the C(3)–C(11) and C(5)–C(13) bonds being only *ca*. 8 and 5° respectively. Here the conformation is stabilized by intramolecular N–H · · · O and C–H · · · O hydrogen bonds, the former producing the *syn* relationship between the *N*-oxide oxygen O(12) and the amido nitrogen N(14). The bonding in the thiadiazole ring differs noticeably from that observed in **3**, there being a pattern of delocalization that extends from C(3) *via* S(1) to N(4).

The molecules pack as hydrogen-bonded dimer pairs that are further loosely linked *via* weak S · · · N interactions to form tapes [Fig. 7(a)]. Adjacent tapes are stacked with the phenyl rings in one tape overlaying the thiadiazole rings in the next [Fig. 7(b)].

Experimental

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 298 instrument in KBr pellets except where noted. ^{1}H NMR spectra were recorded on a Bruker WM 250 spectrometer (250 MHz) and ^{13}C NMR spectra were recorded on a Bruker AM 300 (75.5 MHz). Mass spectra were recorded on an AEI MS12 instrument using electron impact ionization. Light petroleum refers to the fraction bp 40–60 °C.

Amidoximes,[5] and their *O*-acetyl,[15] *O*-benzoyl[16] and *O*-carbamoyl[16] derivatives were made by literature procedures. *O*-Trimethylsilylbenzamidoxime[17] was created *in situ*.

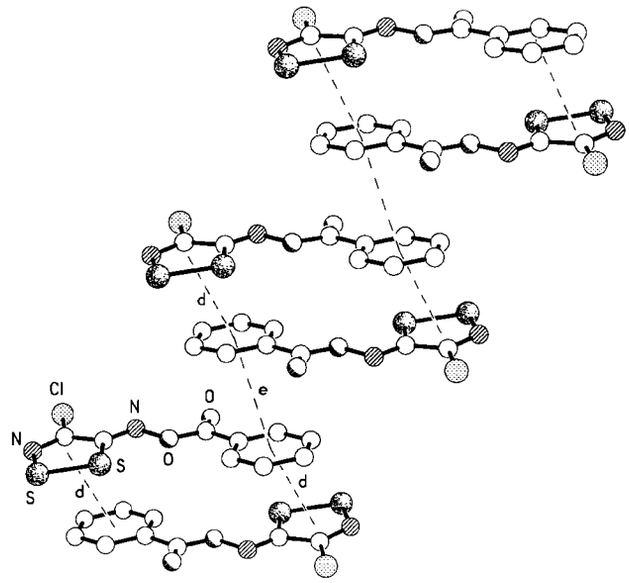


Fig. 5 Part of one of the stepped stacks of dimers present in the structure of **13**. The centroid · · · centroid and mean interplanar separations are: (**d**) 3.77, 3.44; (**e**) 3.83, 3.41 Å; the phenyl and dithiazole rings are inclined by *ca*. 6°.

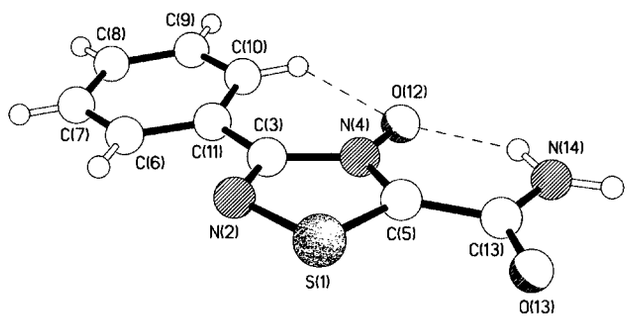


Fig. 6 The molecular structure of **13**. Selected bond lengths (Å) are: S(1)–N(2) 1.640(2), S(1)–C(5) 1.679(2), N(2)–C(3) 1.309(3), C(3)–N(4) 1.410(3), C(3)–C(11) 1.458(3), N(4)–O(12) 1.301(2), N(4)–C(5) 1.341(3), C(5)–C(13) 1.472(3), C(13)–O(13) 1.235(3), C(13)–N(14) 1.324(3).

^{15}N Labelled benzamidoxime

^{15}N Labelled ammonia (1 ml of 30% aqueous ammonia, 95 atom% ^{15}N) was added to a solution of benzoylhydroxamic acid chloride (311 mg, 2 mmol) in ethanol (10 ml). The reaction mixture was stirred at RT for 1 h and the solvent was evaporated under reduced pressure. The residue was dissolved in 10% aqueous hydrochloric acid, filtered, neutralized with aqueous sodium hydroxide and extracted with ether. The solvent was evaporated and the residue was crystallized from water to give the title compound, mp 79–80 °C (200 mg, 74%); *m*/*z* 194 (M^+); δ_C[$(CD_3)_2SO$] 126.7, 128.4, 130.5 and 131.5 (Ph), 154.3 (C–$^{15}NH_2$, $^1J_{^{13}C-^{15}N}$ = 14.9 Hz).

5-Cyano-3-phenyl-1,2,4-thiadiazole 3

4,5-Dichloro-1,2,3-dithiazolium chloride (417 mg, 2 mmol) was added to a solution of benzamidine (free base; 240 mg, 2 mmol) in DCM (10 ml). Pyridine (0.32 ml, 4 mmol) was added and the mixture was stirred at RT for 16 h. The solvent was removed under reduced pressure and flash chromatography on silica with gradient elution from light petroleum to DCM gave 4-chloro-5*H*-1,2,3-dithiazole-5-thione **7** (106 mg, 64%) and the title compound **3** (86.4 mg, 23%), mp 110–111 °C (Found: C, 57.5; H, 2.4; N, 22.1; M^+, 187.0204. $C_9H_5N_3S$ requires C, 57.7; H,

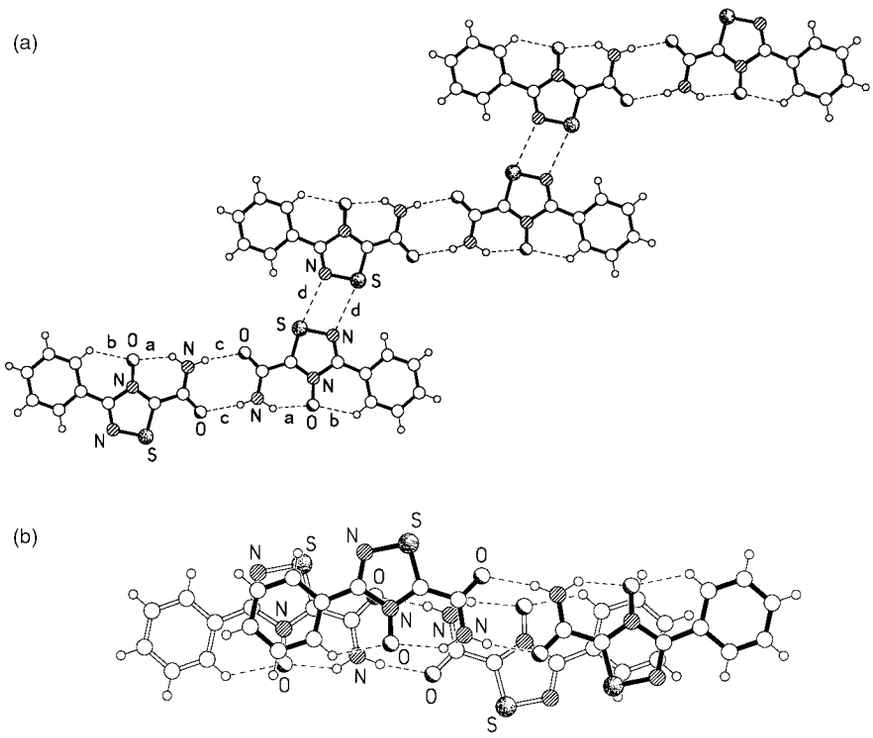


Fig. 7 (a) Part of one of the loosely linked tapes of hydrogen bonded dimers in the structure of **14**. The hydrogen bonding geometries [X · · · O], [H · · · O] distances (Å), [X–H · · · O] angle (°) are: (**a**) 2.72, 1.95, 142; (**b**) 2.84, 2.19, 124; (**c**) 2.86, 1.97, 168. The non-bonded S · · · N distance (**d**) is 3.41 Å. (b) The stacking of the hydrogen bonded dimers; the mean interplanar separation between the phenyl and thiadiazine ring systems is 3.50 Å, the rings being inclined by *ca*. 8°.

2.7; N, 22.4%; *M*, 187.0204); ν_{max}/cm^{-1} (CCl_4) 3073, 1474, 1446, 1410, 1260, 1139, 713, 690; δ_H($CDCl_3$) 8.29–8.36 (m, 2H, 3-H), 7.54 (d, 2H, *J* 2.0 Hz, 2-H), 7.52 (d, 1H, *J* 2.2 Hz, 4-H); δ_C($CDCl_3$) 111.7 (CN), 129.1 (CH), 129.9 (CH), 132.0, 132.3 (CH), 159.3 (*C*-CN), 174.5 (*C*-Ph); *m*/*z* 187 (M^+, 100%), 135 ($PhCNS^+$, 67), 103 ($PhCN^+$, 18), 77 (Ph^+, 16).

Crystal data for 3. $C_9H_5N_3S$, $M = 187.2$, monoclinic, space group $P2_1/c$ (no. 14), $a = 8.743(2)$, $b = 5.301(1)$, $c = 18.959(5)$ Å, $\beta = 102.75(2)°$, $Z = 4$, $D_c = 1.451$ g cm^{-3}, μ(Cu-Kα) = 29.4 cm^{-1}, $F(000) = 384$, $T = 293$ K; orange–red spheres, diameter 0.33 mm, Siemens P4/PC diffractometer, ω-scans, 1371 independent reflections. The structure was solved by direct methods and the non-hydrogen atoms were refined anisotropically using full matrix least-squares based on F^2 to give $R_1 = 0.035$, $wR_2 = 0.096$ for 1262 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 126°$] and 107 parameters. CCDC reference number 207/346.

3-Aryl-5-cyano-1,2,4-thiadiazole 4-oxides

General procedure. A mixture of 4,5-dichloro-1,2,3-dithiazolium chloride **1** (1.51 g, 7.2 mmol) and amidoxime derivative (7.2 mmol) in DCM (40 ml) was stirred at ambient temperature for 24 h. Then pyridine (1.16 ml, 14.4 mmol) was added and the mixture was stirred for a further 10 h. The solvent was removed under reduced pressure, the products were isolated by flash chromatography on silica with gradient elution from light petroleum to dichloromethane. Yields are given in Tables 1 and 2.

5-Cyano-3-phenyl-1,2,4-thiadiazole 4-oxide 5. Mp 142–144 °C (decomp.) (Found: C, 52.9; H, 2.5; N, 20.6; S, 15.8. $C_9H_5N_3OS$ requires: C, 53.2; H, 2.5; N, 20.7; S, 15.8%); ν_{max}/cm^{-1} 2250 (CN), 1600 (C=N), 1485, 1450, 1360, 1320, 1260, 1100, 1030, 930, 870, 830, 770, 680; δ_H[$(CD_3)_2CO$] 7.54–7.66 and 8.41–8.44 (m, 5H, Ph); δ_C[$(CD_3)_2CO$] 108.7 (CN), 127.7, 129.3, 129.5 and 133.2 (Ph), 136.2 (C-CN), 161.2 (C-Ph); *m*/*z* 203 (M^+, 45%), 187 ($M^+ - O$, 21), 173 ($M^+ - NO$, 4), 135 (PhCNS, 62), 103 (PhCN, 55).

5-Cyano-3-phenyl-1,[^{15}N]2,4-thiadiazole 4-oxide (91% ^{15}N). *m*/*z* 204 (M^+), 188 ($M^+ - O$), 174 ($M^+ - NO$), 136 (PhCNS), 104 (PhCN); δ_C[$(CD_3)_2CO$] 108.3 (CN), 126.5 (*ipso*, $^2J_{^{13}C-^{15}N}$ 5.2 Hz), 128.0, 128.3 and 131.8 (Ph), 136.2 (C-CN), 159.3 (C-Ph).

4-Chloro-5*H*-1,2,3-dithiazol-5-one **6**, mp 37–38 °C, and 4-chloro-5*H*-1,2,3-dithiazole-5-thione **7**, mp 77–79 °C, were identical with authentic specimens.[6]

5-Cyano-3-(4-methylphenyl)-1,2,4-thiadiazole 4-oxide 11a. Mp 96–98 °C (decomp.) (Found: C, 55.3; H, 3.1; N, 19.3; S, 14.8. $C_{10}H_7N_3OS$ requires C, 55.3; H, 3.3; N, 19.3; S, 14.8%); ν_{max}/cm^{-1} 2860 (CH_3), 2230 (CN), 1610 (C=N), 1510, 1460, 1410, 1360, 1180, 820; δ_H[$(CD_3)_2CO$] 2.42 (s, 3H, CH_3), 7.40 (d, 2H, Ar, *J* 8.8 Hz), 7.63 (d, 2H, Ar, *J* 8.9 Hz); δ_C[$(CD_3)_2CO$] 21.6 (CH_3), 110.2 (CN), 128.2, 128.9, 131.0 and 133.0 (Ar), 144.9 (C-CN), 156.0 (C-Ar); *m*/*z* 217 (M^+, 59%), 201 ($M^+ - O$, 28), 187 ($M^+ - NO$, 7), 149 (ArCNS, 85), 117 (ArCN, 52).

5-Cyano-3-(4-methoxyphenyl)-1,2,4-thiadiazole 4-oxide 11b. Mp 204–206 °C (decomp.) (Found: C, 51.8; H, 2.9; N, 17.8. $C_{10}H_7N_3O_2S$ requires C, 51.5; H, 3.0; N, 18.0%); ν_{max}/cm^{-1} 2950 (CH_3), 2230 (CN), 1600 (C=N), 1490, 1370, 1310, 1090, 1020, 830; δ_H($CDCl_3$) 3.91 (s, 6H, CH_3), 7.01 (d, 2H, Ar, *J* 9.0 Hz), 8.49 (d, 2H, Ar, *J* 9.0 Hz); δ_C($CDCl_3$) 56.0 (CH_3), 109.2 (CN), 114.5, 119.4, 130.4 and 136.7 (Ar), 159.5 (C-CN), 162.5 (C-Ar); *m*/*z* 233 (M^+, 69%), 217 ($M^+ - O$, 32), 202 ($M^+ - NO$, 7), 165 (ArCNS, 83), 133 (ArCN, 49), 103 (22).

5-Cyano-3-(4-dimethylaminophenyl)-1,2,4-thiadiazole 4-oxide 11c. Mp 96–98 °C (decomp.) (Found: C, 53.5; H, 4.0; N, 22.8; S, 13.2. $C_{11}H_{10}N_4OS$ requires C, 53.6; H, 4.1; N, 22.8; S, 13.0%); ν_{max}/cm^{-1} 2210 (CN), 1610 (C=N), 1530, 1460, 1410, 1370, 1190, 1070, 950, 820; δ_H[$(CD_3)_2CO$] 3.04 (s, 6H, CH_3), 6.77 (d, 2H, Ar, *J* 8.5 Hz), 7.48 (d, 2H, Ar, *J* 8.6 Hz); δ_C[$(CD_3)_2CO$] 40.1 (CH_3),

98.1 (CN), 112.6, 121.0, 130.7 and 134.1 (Ar), 153.8 (C-CN), 165.0 (C-Ar); *m/z* 246 (M^+, 48%), 230 ($M^+ - O$, 22), 216 ($M^+ - NO$, 2), 178 (ArCNS, 92), 146 (ArCN, 42).

Deoxygenation of *N*-oxide 5

A solution of triphenylphosphine (393 mg, 1.5 mmol) in DCM (10 ml) was added to a solution of *N*-oxide **5** (203 mg, 1 mmol) in DCM (20 ml). The reaction mixture was stirred for 20 h at RT. The solvent was evaporated under reduced pressure and flash chromatography on silica with gradient elution (light petroleum–DCM) gave 5-cyano-3-phenyl-1,2,4-thiadiazole **3** (150 mg, 80%) identical with that described above. Phosphorus trichloride in hot DCM converted **5** into **3** in similar yield.

5-Benzoyloxyimino-4-chloro-5*H*-1,2,3-dithiazole 13

To a mixture of 4,5-dichloro-1,2,3-dithiazolium chloride **1** (513 mg, 2.5 mmol) and *O*-benzoylhydroxylamine (340 mg, 2.5 mmol) in DCM (15 ml), pyridine (0.4 ml, 5 mmol) was added and stirred for 10 h. The solvent was removed under reduced pressure, and flash chromatography of the residue on silica with gradient elution from light petroleum to dichloromethane gave the *title compound* **13** as a yellow solid (230 mg, 34%), mp 169–171 °C (Found: C, 39.4; H, 1.9; N, 10.2. $C_9H_5ClN_2O_2S_2$ requires C, 39.6; H, 1.8; N, 10.3%); ν_{max}/cm^{-1} 2920 (CH), 1750 (C=O), 1650 (C=N), 1530, 1450, 1250, 1220, 1070, 1050, 1020, 780 (C–Cl), 720; $\delta_H(CDCl_3)$ 7.08–7.29 and 7.69–7.73 (m, 5H, Ph); $\delta_C(CDCl_3)$ 127.6, 128.8 (CH), 129.9 (CH), 134.0 (CH), 141.3, 161.3, 162.3; *m/z* 272 (M^+, 59%), 162 (4), 122 (13), 105 (100), 77 (32) (Found: M^+, 271.9495. $C_9H_5ClN_2O_2S_2$ requires *M*, 271.9481).

Crystal data for 13. $C_9H_5N_2O_2S_2Cl$, $M = 272.7$, monoclinic, space group *I*2/*a* (no. 15), $a = 12.854(1)$, $b = 8.147(1)$, $c = 21.431(4)$ Å, $\beta = 102.85(2)°$, $Z = 8$, $D_c = 1.656$ g cm^{-3}, μ(Mo-Kα) = 7.14 cm^{-1}, $F(000) = 1104$, $T = 293$ K; yellow prisms, 0.47 × 0.37 × 0.20 mm, Siemens P4/PC diffractometer, ω-scans, 1858 independent reflections. The structure was solved by direct methods and the non-hydrogen atoms were refined anisotropically using full matrix least-squares based on F^2 to give $R_1 = 0.056$, $wR_2 = 0.136$ for 1365 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 50°$] and 133 parameters. CCDC reference number 207/346.

3-Phenyl-1,2,4-thiadiazole-5-carboxamide 4-oxide 14

A mixture of nitrile **5** (203 mg, 1 mmol) in aqueous hydrochloric acid (10%, 30 ml) was refluxed for 10 min, then cooled, filtered, diluted with water (30 ml) and extracted with ether (3 × 40 ml) and then dichloromethane (80 ml). The combined extracts were washed with water and dried over $MgSO_4$. Evaporation gave the *title compound* **14** (130 mg, 60%), mp 199–200 °C (from DCM) (Found: C, 48.7; H, 3.2; N, 14.5. $C_9H_7N_3O_2S$ requires C, 48.9; H, 3.2; N, 14.5%); ν_{max}/cm^{-1} 3250 and 3110 (NH_2), 1680 (C=O), 1485, 1430, 1370, 1260, 1130, 1030, 780, 670; $\delta_H(CDCl_3)$ 6.45 (br s, 1H, NH), 7.55–7.65 and 8.45–8.58 (m, 5H, Ph); $\delta_C(CDCl_3)$ 127.2, 128.7 (CH), 128.7 (CH), 132.3 (CH), 156.9, 158.1, 163.0; *m/z* 221 (M^+, 31%), 205 ($M^+ - O$, 5), 148 (11), 135 (46), 104 (100) (Found: M^+, 221.0266. $C_9H_7N_3O_2S$ requires *M*, 221.0259).

Crystal data for 14. $C_9H_7N_3O_2S$, $M = 221.2$, monoclinic, space group $P2_1/c$ (no. 14), $a = 11.631(1)$, $b = 5.289(1)$, $c = 16.340(3)$ Å, $\beta = 105.01(1)°$, $Z = 4$, $D_c = 1.514$ g cm^{-3}, μ(Cu-Kα) = 28.5 cm^{-1}, $F(000) = 456$, $T = 293$ K; orange needles, 1.00 × 0.30 × 0.15 mm, Siemens P4/PC diffractometer, ω-scans, 1566 independent reflections. The structure was solved by direct methods and the non-hydrogen atoms were refined anisotropically using full matrix least-squares based on F^2 to give $R_1 = 0.044$, $wR_2 = 0.129$ for 1453 independent observed absorption corrected reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 126°$] and 145 parameters. CCDC reference number 207/346.

Acknowledgements

We thank the Royal Society, the *Dirección General de Enseñanza Superior* of Spain (DGES Project ref. PB96-0101) and MDL Information Systems (UK) LTD for financial support, the Wolfson Foundation for establishing the Wolfson Centre for Organic Chemistry in Medical Science at Imperial College and Dr R. F. English for some early experiments and Mr R. Sheppard for expert help with the NMR spectroscopy.

References

1 A. R. Katritzky and J. M. Lagowski, in *Comprehensive Heterocyclic Chemistry I*, ed. A. R. Katritzky and C. W. Rees, Pergamon, Oxford, 1984, vol. 5, p. 55.
2 L. M. Weistock and I. Shinkai, in ref. 1, vol. 6, p. 525.
3 D. J. Wilkins and P. A. Bradley, in *Comprehensive Heterocyclic Chemistry II*, ed. A. R. Katritzky, C. W. Rees and E. F. V. Scriven, Pergamon, Oxford, 1996, vol. 4, p. 352.
4 O. A. Rakitin, C. W. Rees and O. G. Vlasova, *Chem. Commun.*, 1996, 1273.
5 F. Eloy and R. Lenaers, *Chem. Rev.*, 1962, **62**, 155.
6 R. Appel, H. Janssen, M. Siray and F. Knoch, *Chem. Ber.*, 1985, **118**, 1632.
7 (*a*) C. W. Rees, *J. Heterocycl. Chem.*, 1992, **29**, 639; (*b*) T. Besson and C. W. Rees, *J. Chem Soc., Perkin Trans. 1*, 1995, 1659; (*c*) R. F. English, O. A. Rakitin, C. W. Rees and O. G. Vlasova, *J. Chem. Soc., Perkin Trans. 1*, 1997, 201; K. Emayan, R. F. English, P. A. Koutentis and C. W. Rees, *J. Chem Soc., Perkin Trans. 1*, 1997, 3345; (*e*) L. S. Konstantinova, O. A. Rakitin, C. W. Rees, S. Sivadasan and T. Torroba, *Tetrahedron*, 1998, **54**, 9639.
8 R. F. English, PhD Thesis, University of London, 1989.
9 K. T. Potts and R. Armbruster, *J. Heterocycl. Chem.*, 1972, **9**, 651.
10 G. W. Buchanan and B. A. Dawson, *Can. J. Chem.*, 1976, **54**, 790 and 1978, **56**, 2200.
11 T. Besson, J. Guillard, C. W. Rees and V. Thiéry, *J. Chem Soc., Perkin Trans. 1*, 1998, 889.
12 H. W. Roesky, K. Keller and J. W. Bats, *Angew. Chem., Int. Ed. Engl.*, 1983, **22**, 881.
13 T. Chivers, M. Parvez and P. Zoricak, *Z. Naturforsch., Teil B*, 1997, **52**, 557.
14 H. W. Roesky, J. Sundermayer, J. Schmikowiak, T. Gries, M. Noltemeyer and G. M. Sheldrick, *Z. Naturforsch., Teil B*, 1986, **41**, 162.
15 O. Schulz, *Chem. Ber.*, 1885, **18**, 1080.
16 F. Tiemann and P. Kruger, *Chem. Ber.*, 1884, **17**, 1685.
17 A. B. Goel and V. D. Gupta, *J. Organomet. Chem.*, 1974, **72**, 171.

Paper 9/04386A